

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44bis.3(c) and 72.2)

To:

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Date of mailing (day/month/year)
08 September 2006 (08.09.2006)

Applicant's or agent's file reference
PH-2347-PCT

IMPORTANT NOTIFICATION

International application No.
PCT/JP2004/018339

International filing date (day/month/year)
02 December 2004 (02.12.2004)

Applicant
JAPAN SCIENCE AND TECHNOLOGY AGENCY et al

1. Transmittal of the translation to the applicant.

- ☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).
- ☒ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

EP, KR

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Yoshiko Kuwahara

TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PH-2347-PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2004/018339	International filing date (day/month/year) 02.12.2004	Priority date (day/month/year) 11.12.2003
International Patent Classification (IPC) or national classification and IPC A61L27/38, C12N5/06		
Applicant JAPAN SCIENCE AND TECHNOLOGY AGENCY		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.	
2. This REPORT consists of a total of <u>6</u> sheets, including this cover sheet.	
3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input checked="" type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) <u>1 flexible disk</u> , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).	
4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application	

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/IP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

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Box No. 1

Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
 - ☐ publication of the international application (Rule 12.4)
 - ☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ the international application as originally filed/furnished

- ☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

- ☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

- ☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-9	YES
	Claims		NO
Inventive step (IS)	Claims	1-9	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: JP 2001-512304 A (Osiris Therapeutics, Inc.),
21 August 2001

Document 2: S. MARLOVITS et al., "Tissue engineering of
human articular cartilage in rotating-wall
vessels," International Journal of
Artificial Organs, July 2002, Vol. 25, No.
7, page 676

Document 3: S. MARLOVITS et al., "Three-dimensional
culture of human articular chondrocytes in
rotating-wall vessels," FASEB Journal, 1999,
Vol. 13, No. 4, part 1, page A427

Document 3: T. L. PREWETT et al., "Three-dimensional
culture of bovine chondrocytes in rotating-
wall vessels," In Vitro Cellular and
Developmental Biology Animal, 1994, Vol. 30
A, No. 3, part 2, page 109

Document 4: L. E. FREED et al., "Microgravity tissue
engineering," In Vitro Cellular and
Developmental Biology Animal, 1994, Vol. 33,
No. 5, pages 381 to 385

Document 6: JP 2003-009852 A (Mitsubishi Heavy
Industries, Ltd.), 14 January 2003

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability:
citations and explanations supporting such statement

Document 1 cited in the international search report discloses compositions for forming human chondrocytes within a test tube, said compositions comprising dexamethasone, TGF- β 1 and mesenchymal stem cells that have been disposed in a three-dimensional arrangement.

Meanwhile, documents 2 to 4 cited in the international search report indicate that the use of a rotating wall vessel (RWV) during the culturing process promoted both the differentiation of articular cartilage and the production of extracellular matrices that are specific to cartilage.

In addition, document 5 cited in the international search report indicates that the most glycosaminoglycan was secreted in cases when the chondrocytes were cultured in a pseudo microgravity environment (refer to the abstract and the like).

Furthermore, document 6 cited in the international search report indicates that multipotent stem cells acquired from bone marrow were induced to differentiate into bone and cartilage by mixing dexamethasone and TGF- β into the culture medium and then culturing said multipotent stem cells in a rotating environment (refer to paragraphs [0016] and [0019]).

Claims 1 to 9

Documents 1 to 6 do not mention a technique for constructing cartilage tissue by culturing myeloid cells in a pseudo microgravity environment.

Furthermore, the invention disclosed in document 6 employs a centrifugal culture device in order to induce the myeloid cells to differentiate into cartilage (refer to paragraph [0019]), and thus it is apparent that the

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Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

author of document 6 considered the application of a mechanical stimulus to be important in order to induce the myeloid cells to differentiate into cartilage. On the other hand, the inventions set forth in the present application were found to be capable of promoting the differentiation of myeloid cells into chondrocytes while also promoting the construction of cartilage tissue from myeloid cells as a result of culturing the myeloid cells in a pseudo microgravity environment, and it would not have been easy for even a person skilled in the art to conceive of the effects in question.

Such being the case, the inventions set forth in claims 1 to 9 are novel and involve an inventive step in relation to documents 1 to 6.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

* If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."